IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Chenevert, et al.
Serial No.:   10/807,531   Group No.: 3737
Filed: 03/23/2004   Examiner: Mehta
Entitled: **NONINVASIVE METHOD TO DETERMINE FAT CONTENT OF TISSUES USING MRI**

DECLARATION OF Thomas Chenevert, Ph.D.

Examiner Hiriyanna:

I, Thomas Chenevert, Ph.D., hereby declare and state, under penalty of perjury, that:

1. I am an inventor of the above-named patent application (hereinafter "present application"). I am a Professor in the Departments of Radiology at the University of Michigan Medical School. I have worked in the field of magnetic resonance imaging for many years and have numerous publications in this field.

2. I have reviewed the Office Action mailed dated September 30, 2008, where the Examiner rejected Claims 1-8, 10-17, 19 and 20 as being anticipated by Levenson, et al., Am. J. Roentgenology 156:307-312 (hereinafter, "the Levenson reference").

3. I understand that in the Response filed with this Declaration, Claims 10-18 and 20 are canceled, and Claim 1 is amended such that it recites:

1.   A system, comprising:
      a)   a sample,
      b)   data obtained from an MRI device, wherein said data comprise at least one pair of consecutive in-phase and out-phase echoes of said sample collected and reconstructed into images in magnitude format, and
      c)   software embodied on a computer readable medium, wherein said software is configured to receive said data obtained from said MRI device, wherein said software is further configured to process said at least one pair of consecutive in-phase and out-phase echoes reconstructed into images in magnitude format, wherein said processing comprises determining the percent of fat content within said sample as between 0 to 100%, wherein

said software is further configured to display said determined fat percentage within said sample.

4.   The Levenson reference does not teach or describe how to determine fat content percentage from at least one pair of consecutive in-phase and out-phase echoes of a sample, where the determined fat content percentage is between 0 to 100%. For example, true fat content of approximately 20% fat is indistinguishable from 80% fat content by applying the approach described in the Levenson reference. Indeed, the Levenson reference's approach for determining fat content percentage within a sample does not remove the ambiguity of determining whether the fat content is above or below 50%.

In particular, the Levenson reference's use of equation (1) on page 309, column 1, is based on well-established expressions to estimate fat content given magnitude in-phase and out-phase data, but equation (1) is correct only when there are no relaxation effects and one knows *a priori* the fat content is below 50%. Equation (2), described on page 309, column 1, incorporates factors in the event of relaxation effects, but equation (2) and associated text does not claim to remedy effects of relaxation.

The Levenson reference describes the inherent limitations for removing the ambiguity of determining whether the fat content is above or below 50%:

> Figure 2 also illustrates the second problem associated with equation 1. Because MR imagers typically display only the magnitude of the reconstructed image, **there is an intrinsic ambiguity in applying equation 1 to data**. Although S_{out} accurately reflects the difference in the water and fat signals, **it is not possible to identify whether the fat or the water is the dominant signal**. Mathematically, this means that we do not know the correct sign for S_{out} in equation 1. As a result, for f0 > 0.5, we will in fact be identifying the water fraction, 1 - f0 (shown as the dotted curves in Fig. 2). When this study was done, we did not have the capability of determining the sign of S_{out} from the phase of the image. (page 309) (emphasis added)
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> . . .
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> In using the f given by equation 1 as "fat fraction," **we tacitly have assumed that the fat fraction is always less than the water fraction**. On the basis of the biopsy results, it is likely that six of our patients had fat fractions greater than 0.5. As noted, this problem may have reduced our correlation coefficient from .96 to
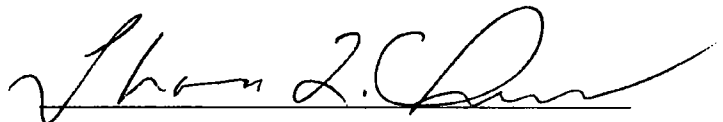
.86 (Fig. 3). A robust application of the method clearly should include a phase correction scheme (e.g., [3, 10]) so that the ambiguity is removed. (page 311) (emphasis added)

Accordingly, application of the approach described in the Levenson reference yields accurate fat content percentage values only if true fat content is in the range 0 to about 40%. Contrarily, if true fat content is between about 40% to 100%, application of the approach described in the Levenson reference yields fat content percentage values in gross error.

5.   During the course of preparing the present invention, experiments were conducted demonstrating determination of fat content percentage from at least one pair of consecutive in-phase and out-phase echoes of a sample, where the determined fat content percentage is between 0 to 100%. Indeed, Examples II, III and IV and Figures 3-7 of the present invention demonstrate determination of fat content percentage using the system described in Claim 1, where the fat content percentage is determined on a scale of 0 to 100%. Unlike the Levenson reference, the plots shown in Figures 3 and 4 are not simulations and represent for the first time determination of fat content percentage above 50% derived from magnitude data.

6.   I further declare that all statements made herein are of my own knowledge, are true, and that all statements are made on information and belief that are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 Title 18 of the United States Code, and that such willful statements may jeopardize the validity of the application of any patent issued thereon.

Dated: 3/25/2009

Thomas Chenevert, Ph.D.